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TITLE: Determinants of Weight Gain in Women with Early-Stage Breast Cancer

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13. SUPPLEMENTARY NOTES

14. ABSTRACT. Weight gain after breast cancer diagnosis is common, and has been associated with poorer prognosis. The goals of the study are to examine weight gain relation to treatment-related changes in sex hormone levels, and in relation to genetic polymorphisms in sex hormone pathways, accounting for potential interactions with energy balance, psychosocial factors, tumor characteristics, cancer treatment, and medication use. A prospective longitudinal study of weight gain is being conducted in 215 stage I to IIIA breast cancer patients. During the first year of this grant, baseline and followup questionnaires were developed. Other recruitment materials developed included a consent script, a study brochure, instruction sheets, and data collection checklists. Study personnel were trained in consenting and recruitment of patients. Protocols for biospecimen collection were developed, which includes collection of serum, plasma, buffy coats, red blood cells, and overnight urine specimens. In collaboration with the departments of Clinical Research Services and the Information Technology, study databases were developed for tracking of patients, as well as for double entry of all data collected by survey. Participant recruitment using consent forms with DOD language began January 2007 after obtaining institutional IRB and USAMRMC Human Research Protections approval. Thirty seven participants have been enrolled using this consent form. The study will help identify women who are most susceptible to weight gain after being diagnosed with breast cancer, based on biologic characteristics as well as modifiable factors.

15. SUBJECT TERMS
Sex hormone, genetic polymorphisms, weight gain, cohort study, diet, physical activity, psychosocial factors.

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1. Introduction

Weight gain after breast cancer diagnosis is very common, occurring in 50-95% of early stage patients undergoing adjuvant chemotherapy, and has been associated with poorer prognosis. Potentially important contributors to this weight gain may be treatment-related reductions in ovarian function and/or increases in cortisol level due to physical and psychological stress. Since sex hormones and glucocorticoids regulate body weight and adipose tissue distribution, we hypothesize that sex hormones and cortisol play a role in treatment-induced weight gain, and that complex interactions exist with genetic susceptibility, lifestyle, and psychosocial factors. The goals of the study are to examine post-diagnostic weight change and: 1) changes in sex hormone and cortisol levels; 2) genetic polymorphisms in sex hormone pathways; 3) energy intake, physical activity, and psychosocial factors; and 4) characteristics of the cancer and treatments received. A prospective longitudinal study of weight gain is being conducted in 290 patients, aged 35 to 75 years, with non-metastatic breast cancer (Stage I to IIIA). After informed consent, we are collecting serial biospecimens and survey data, to measure hormone levels and genetic polymorphisms, and to assess menopausal status, anthropometry, diet, physical activity, and psychological variables (fatigue, depression, social support) at baseline, 6, and 12 months. These factors will be evaluated in relation to weight changes during and following therapy. This study will be the first to comprehensively examine predictors and modulators of post-diagnostic weight gain in women with breast cancer using a multidisciplinary approach encompassing hormonal changes, genetic polymorphisms, and psychosocial factors. The outcome of this research may shed light on why so many women suffer weight gain after breast cancer and will help guide the development of interventions targeting modifiable risk factors.

2. Body

Task 1: Study Protocol Revisions, Months 1 to 6

Study protocols and the consent form were revised to include DOD elements and were submitted to the USAMRMC Office of Research Protections, Human Research Protections Office (ORP HRPO) for review. Local IRB approval and approval from USAMRMC ORP HRPO was obtained January 8th, 2007.

Task 2. Develop databases with Clinical Research Service and Information Technology department at RPCI, months 1-6.

In collaboration with the Clinical Research Services and Information Technology department at Roswell Park, a tracking database has been developed which tracks for each potential participant their study eligibility and participation status. For each participant, the system also tracks specimen collection, as well as allows for entry of all data collected by survey. The database developed uses the eResearch Technology (eRT), eData Management, eStudy Conduct, eSafety Net software products as well as various other RPCI custom applications connected to eRT via Microsoft ODBC technology. The database is currently interfaced to RPCI's hospital information system (demographics), and the RPCI Cerner lab system (lab results), which allows all of this information to transfer electronically. The database management system is Oracle 9i. Backups of the study data to tape are performed nightly and stored in a separate physical location from the servers themselves. Double data entry of all data collected is performed.

Task 3. Train study personnel to consent patients, month 1.

A study co-ordinator was hired and trained to consent patients into the study from the breast clinic at Roswell Park Cancer Institute.

Task 4. Study Recruitment, Months 6-18; Participant Followup, Months 7 to 30.

Recruitment of participants who participate in the Institutes DataBank and BioRepository using consent forms with DOD language was initiated in Jan, 2007. To date (4/24/07), 37 participants have been enrolled. From this group there were 2 withdrawals leaving 35 active participants. Reasons for the withdrawal were 1) patient elected not to receive any of her cancer care treatment at Roswell Park, so she was no longer interested in participating in the study, and 2) one patient changed her mind about participating because it sounded like too much time commitment. The ethnicity/race of participants were 33 White/Caucasian (2 withdrawals), and 4 Black/African American.

Recruitment into the study, prior to DOD approval, began April 2006. The intent will be to reconsent these participants using the DOD approved consent forms. To date (4/24/07), 131 incident breast cancer cases with Stage I to IIIa disease have been enrolled onto the study, with 11 withdrawals (8.3%), leaving 120 active participants.

The ethnicity/race of participants recruited thus far are:

Caucasian (n=115, withdrawn N=10)

Black (n=14, withdrawn n=1)

Native American (n=2).

Questionnaires provided for self-completion at home

We are in the process of collecting data on dietary intake, physical activity, and psychosocial factors through questionnaires administered at baseline, 6 months, and at 12 months.

Measurement of weight, height, and body composition

Protocols to measure body composition and weight in the Roswell Park Breast clinic was established using the Tanita Body Composition analyzer, which uses the tetrapolar bioelectrical impedance technique. As well, protocols were established with clinical staff in the Breast Clinic to measure waist and hip circumferences on all newly diagnosed breast cancer patients at baseline and at followup visits.

Collection of blood and urine samples for sex hormone and cortisol determination

Protocols for the collection and processing of fasting blood samples prior to surgery/treatment were developed and include banking of serum, plasma, buffy coat, and red blood cells. As well, presurgical overnight urine specimens were collected, which is accompanied by a specimen questionnaire that was developed, which asks about lifestyle, diet, and medication use in the last 2 days. Currently, fresh whole blood is sent to Labcorp for determination of HbA1C results. Serum and plasma are being stored to allow for future determination of sex hormone and cortisol levels. Originally we had planned to begin shipping serum samples periodically to Labcorp to determine hormone levels beginning in month 6, but

to reduce laboratory error we will instead wait until followup is complete and have baseline, 6 months, and 1 year samples assayed simultaneously.

Task 5. Data Management, Months 6 to 31.

We are in the process of double entering all our data into study databases. This is done by at least 2 different individuals, and periodically the two sets of data entered are compared and differences are flagged for further followup.

Task 6. Measurement of hormone levels, Months 12 to 31.

This task has not yet begun. Currently, fresh whole blood is sent to Labcorp for determination of HbA1C results. Serum and plasma are being stored to allow for future determination of sex hormone and cortisol levels. Originally we had planned to begin shipping serum samples periodically to Labcorp to determine hormone levels beginning in month 6, but to reduce laboratory error we will instead wait until followup is complete and have baseline, 6 months, and 1 year samples assayed simultaneously.

Task 7. Postdoctoral Training, Months 1-36

Developmental meetings are held weekly and on an as needed basis to discuss progress and career development with Dr. Christine Ambrosone, the primary mentor. Meetings with all research mentors occur once every 6 months. I attended the annual meeting of the American Association for Cancer Research, held in Los Angeles CA, April 15 to 18th, 2007, and was the co-chair for the Tenth Annual Grant Writing Workshop for Associate Members, Professional Advancement Session, which was held on April 14, 2007. I plan to attend the AACR Molecular Epidemiology Working Group (MEG) sponsored special conference on 'Approaches to Complex Pathways in Molecular Epidemiology' from May 30 to June 2nd, 2007. I continue to attend (and coordinate) the biweekly work-in-progess meetings in epidemiology and chemoprevention that occur within the Department of Cancer Prevention and Control at Roswell Park Cancer Institute, as well as weekly Faculty Forum, Cancer Prevention Grand Rounds, and Medical Grand Rounds seminars.

Task 8. Mount Sinai Center Visit, Month 12

I have not yet visited Dr. Bovbjerg yet at the Mount Sinai Center in NY. We plan to have more followup psychosocial data collected before planning this visit.

Task 9. Interim Analyses, Months 12-30

Not yet started.

Task 10. DNA extraction and Genotyping, Months 14 to 22.

Not yet started. As part of the blood collection protocol, buffy coats are being banked and stored to allow for DNA extraction and genotyping. For participants recruited thus far, we will begin DNA extraction and genotyping in the summer of 2007.

Task 11. Merge genotyping data with data questionnaires and medical records. Month 23.

Not yet performed. We have not yet merged medical records data yet with our survey data, although the clinical data is routinely collected by the Breast Surgery department and is readily available when needed. This task is scheduled for Months 23 to 30 of the grant.

Task 12. Final data analysis, interpretation and reporting, Months 31 to 36.

Not yet performed.

3. Key Research Accomplishments.

None yet.

4. Reportable Outcomes

None yet.

5. Conclusion

In the first year of this grant, baseline and followup questionnaires were finalized for this study, along with a questionnaire to assess recent diet, lifestyle, and medication patterns that may impact blood and urine measures taken. As well, other recruitment materials were developed and finalized including a consent script, a study brochure, instruction sheets, and data collection checklists. Study personnel were trained in consenting and recruitment of patients. Protocols for biospecimen collection were developed, which includes collection of serum, plasma, buffy coats, red blood cells, and overnight urine specimens. In collaboration with the departments of Clinical Research Services and the Information Technology, study databases were developed for tracking of patients, as well as for double entry of all data collected by survey. Participant recruitment using consent forms with DOD language began in January 2007 and as of April 24th, 2007, 37 participants have been enrolled onto the study. We will reconsent participants who were recruited into the study prior to January 2007. In the summer of 2007, we will begin genotyping. Findings from this study will help identify women who are most susceptible to weight gain after being diagnosed with breast cancer, based on biologic characteristics as well as modifiable factors. From a public health viewpoint, findings from this study may indicate ways to improve women's health after breast cancer and to optimize their long-term survival.

6. References

None

7. Appendices

None

8. Supporting Data

None